

**Exhibit B to Accompany the Office Action Mailed on March 7, 2003**

On the following pages are a copy of the initialed Information Disclosure Statement in U.S. Patent Application Serial No. 09/406,293, mailed with an Office Action dated February 28, 2001 (5 pages).

Exhibit B

Subt. For, PTO-1449		Docket Number 103576.166		Application Number 09/460,293 09/460,293	
INFORMATION DISCLOSURE IN AN APPLICATION  (Use several sheets if necessary)		Filing Date September 24, 1999		Applicant Chen, Zhijian H.	
		Group Art Unit 1652			
Sheet	1	OF	5		

## U.S. Patent Documents

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
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## Foreign Patent Documents

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
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## Other Documents (Including Author, Title, Date Pertinent Pages, Etc.)

A1	Alkalay, et al., "In Vitro Stimulation of I $\kappa$ B Phosphorylation Is Not Sufficient to Activate NF- $\kappa$ B", <i>Mol. Cell. Biol.</i> , Vol. 15, No. 3, pp. 1294-1304 (1995)
A2	Alkalay, et al., "Stimulation-Dependent I $\kappa$ B- $\alpha$ Phosphorylation Marks the NF- $\kappa$ B Inhibitor for Degradation via the Ubiquitin-Proteasome Pathway" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 92, pp. 10599-10603 (1995)
A3	Arnason and Ellison, "Stress Resistance in <i>Saccharomyces cerevisiae</i> Is Strongly Correlated with Assembly of a Novel Type of Multiubiquitin Chain" <i>Mol. Cell. Biol.</i> , Vol. 14, No. 12, pp. 7876-7883 (1994)
A4	Auffray, et al., "IMAGE: Integrated Molecular Analysis of the Human Genome and Its Expression" <i>Sciences</i> , Vol. 318, pp. 263-272 (1995)
A5	Auphan et al., "Immunosuppression by Glucocorticoids: Inhibition of NF- $\kappa$ B Activity Through Induction of I $\kappa$ B Synthesis" <i>Science</i> , Vol. 270, pp. 286-290 (1995)
A6	Baeuerle and Henkel, "Function and Activation of NF- $\kappa$ B in the Immune System" <i>Annu. Rev. Immunol.</i> , Vol. 12, pp. 141-179 (1994)
A7	Baldi, et al., "Critical Role for Lysines 21 and 22 in Signal-Induced Ubiquitin-Mediated Proteolysis of I $\kappa$ B- $\alpha$ " <i>Vol. 271, No. 1, pp. 376-379 (1996)</i>
A8	Barroga et al., "Constitutive Phosphorylation of I $\kappa$ B- $\alpha$ by Casein Kinase II" <i>Proc. Natl. Acad. Sci.</i> , Vol. 92, pp. 7637-7641 (1995)
A9	Beg, et al., "Tumor Necrosis Factor and Interleukin-1 Lead to Phosphorylation and Loss of I $\kappa$ B- $\alpha$ : a Mechanism for NF- $\kappa$ B Activation." <i>Mol. Cell. Biol.</i> pp. 3301-3310 (1993)
A10	Belvin, et al., "Cactus Protein Degradation Mediates Drosophila Dorsal-Ventral Signaling" <i>Genes and Dev.</i> , Vol. 9, pp. 783-793 (1995)
A11	Blank, et al., "Molecular Cloning of Mitogen-activated Protein/ERK Kinase Kinases (MEKK) 2 and 3" <i>J. Biol. Chem.</i> , Vol. 271, No. 10, pp. 5361-5368 (1996)
A12	Brockman, J.A., "Coupling of a Signal Response Domain in I $\kappa$ B- $\alpha$ to Multiple Pathways for NF- $\kappa$ B Activation" <i>Mol. Cell. Biol.</i> , Vol. 15, No. 5 (1995), 2808-2818
A13	Brown, et al., "Control of I $\kappa$ B- $\alpha$ Proteolysis by Site-Specific, Signal-Induced Phosphorylation" <i>Science</i> , Vol. 267, pp. 1485-1488 (1995)
A14	Chau, "A Multiubiquitin Chain is Confined to Specific Lysine in a Targeted Short-Lived Protein" <i>Science</i> , Vol. 243, pp. 1576-1583 (1989)

EXAMINER <i>[Signature]</i>	DATE CONSIDERED <i>11/27/01</i>
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B1	Chen, et al., "Multiple Ubiquitin-Conjugating Enzymes Participate in the In Vivo Degradation of the Yeast MATa2 Repressor" <i>Cell</i> , Vol. 74, pp. 357-369 (1993)
B2	Chen, et al., "Signal-Induced Site-Specific Phosphorylation Targets I $\kappa$ B- $\alpha$ to the Ubiquitin-Proteasome Pathway" <i>Genes and Dev.</i> , Vol. 9, pp. 1586-1597 (1995)
B3	Chen, et al., "Site-Specific Phosphorylation of I $\kappa$ B- $\alpha$ by a Novel Ubiquitination-Dependent Protein Kinase Activity" <i>Cell</i> , Vol. 84 (1996), 853-862
B4	Chen and Pickart, "A 25-Kilodalton Ubiquitin Carrier Protein (E2) Catalyzes Multi-ubiquitin Chain Synthesis via Lysine 48 of Ubiquitin" <i>J. Biol. Chem.</i> , Vol. 265, No. 35, pp. 21835-21842 (1990)
B5	Choi, et al., "Ste5 Tethers Multiple Protein Kinases in the MAP Kinase Cascade Required for Mating in <i>S. cerevisiae</i> " <i>Cell</i> , Vol. 78, pp. 499-512 (1994)
B6	Ciechanover, "The Ubiquitin-Proteasome Proteolytic Pathway" <i>Cell</i> , Vol. 79, pp. 13-21 (1994)
B7	Derijard, et al., "Independent Human MAP Kinase Signal Transduction Pathways Defined by MEK and MKK Isoforms" <i>Science</i> , Vol. 267, pp. 662-685 (1995)
B8	Derijard, et al., "JNK1: A Protein Kinase Stimulated by UV Light and Ha-Ras That Binds and Phosphorylates the c-Jun Activation Domain" <i>Cell</i> , Vol. 76, pp. 1025-1037 (1994)
B9	Devary, et al., "NF- $\kappa$ B Activation by Ultraviolet Light Not Dependent on a Nuclear Signal" <i>Science</i> , Vol. 261, pp. 1442-1445 (1993)
B10	Diaz-Meco, "ZPKC Induces Phosphorylation and Inactivation of I kappa B-alpha In Vitro" <i>EMBO J.</i> , Vol. 13, No. 12, pp. 2842-2848 (1994)
B11	DiDonato, et al., "Phosphorylation of I $\kappa$ B $\alpha$ Precedes but IS Not Sufficient for Its Dissociation from NF- $\kappa$ B" <i>Mol. cell. Biol.</i> , Vol. 15, No. 3, pp. 1302-1311 (1995)
B12	Dominguez, et al., "Inhibition of Protein Kinase C $\zeta$ Subspecies Blocks the Activation of an NF- $\kappa$ B-like activity in <i>Xenopus Laevis</i> Oocytes" <i>Mol. Cell. Biol.</i> , Vol. 13, No. 2, pp. 1290-1295 (1993)
B13	Finco, et al., "Inducible phosphorylation of I $\kappa$ B $\alpha$ is not sufficient for its dissociation from NF- $\kappa$ B and is inhibited by protease inhibitors" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 91, pp. 11884-11888 (1994)
B14	Finco and Baldwin, "k $\kappa$ B Site-Dependent Induction of Gene Expression by Diverse Inducers of Nuclear Factor $\kappa$ B Requires Raf-1", <i>J. Biol. Chem.</i> , Vol. 268, No. 24, pp. 17676-17679 (1993)
B15	Finco and Baldwin, "Mechanistic Aspect of NF- $\kappa$ B Regulation: The Emerging Role of Phosphorylation and Proteolysis" <i>Immunity</i> , Vol. 3, pp. 263-272 (1995)
B16	Francis and Corbin, "Structure and Function of Cyclic Nucleotide-dependent Protein Kinases" <i>Annu. Rev. Physiol.</i> , Vol. 56, pp. 237-72 (1994)
B17	Ghosh and Baltimore, "Activation In vitro of NF- $\kappa$ B by Phosphorylation of its Inhibitor I $\kappa$ B" <i>Nature</i> , Vol. 344, pp. 678-682 (1990)
B18	Goldberg, Alfred L., "Functions of the Proteasome: The Lysis at the End of the Tunnel" <i>Science</i> , Vol. 268, pp. 522-523 (1995)

EXAMINER <i>C. P. Miller</i>	DATE CONSIDERED 2/27/01
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C1	Gupta, et al., "Transcription Factor ATF2 Regulation by the JNK Signal Transduction Pathway" <i>Science</i> , Vol. 267, pp. 389-393 (1995)
C2	Haskill, et al., "Characterization of an Immediate-Early Gene Induced in Adherent Monocytes that Encodes I $\kappa$ B-like Activity" <i>Cell</i> , Vol. 65, pp. 1281-1289 (1991)
C3	Henkel, et al., "Rapid Proteolysis of I $\kappa$ B- $\alpha$ is Necessary for Activation of Transcription Factor NF- $\kappa$ B" <i>Nature</i> , Vol. 365, pp. 182-185 (1993)
C4	Hershko and Heller, "Occurrence of a Polyubiquitin Structure in Ubiquitin-Protein Conjugates" <i>Biochem. Biophys. Res. Commun.</i> , Vol. 128, No. 3, pp. 1079-1086 (1985)
C5	Hershko and Ciechanover, "The Ubiquitin System for Protein Degradation" <i>Annu. Rev. Biochem.</i> , Vol. 61, pp. 761-807 (1992)
C6	Hibi, et al., "Identification of an oncoprotein- and UV-responsive protein kinase that binds and potentiates the c-Jun activation domain" <i>Genes and Dev.</i> , Vol. 7, pp. 2135-2148 (1993)
C7	Higgins, et al., "Antisense inhibition of the p65 subunit of NF- $\kappa$ B blocks tumorigenicity and causes tumor regression" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90, pp. 9901-9905 (1993)
C8	Hirano, et al., "MEK Kinase Is Involved in Tumor Necrosis Factor $\alpha$ -Induced NF- $\kappa$ B Activation and Degradation of I $\kappa$ B- $\alpha$ " <i>J. Biol. Chem.</i> , Vol. 271, No. 22, pp. 13234-13238 (1996)
C9	Kumar, A., et al., "Double-Stranded RNA-Dependent Protein Kinase Activates Transcription Factor NF- $\kappa$ B by Phosphorylating I $\kappa$ B" <i>Proc. Natl. Acad. Sci. USA</i> Vol. 91, pp. 6288-6292 (1994)
C10	Kuno, et al., "Identification of an I $\kappa$ B- $\alpha$ - Associated Protein Kinase in a Human Monocytic Cell Line and Determination of its Phosphorylation Sites on I $\kappa$ B- $\alpha$ " <i>Biol. Chem.</i> Vol. 270, No. 46, pp. 27914-27919 (1995)
C11	Lange-Carter, et al., "A Divergence in the MAP Kinase Regulatory Network Defined by MEK Kinase and Raf" <i>Science</i> , Vol. 260, pp. 315-319 (1993)
C12	Li and Sedivy "Raf-1 Protein Kinase Activates the NF- $\kappa$ B Transcription Factor By Disassociating the Cytoplasmic NF- $\kappa$ B-I $\kappa$ B complex" <i>Proc Natl Acad Sci USA</i> , Vol. 90, pp. 9247-9251 (1993)
C13	Lin, et al., "Activation of NF- $\kappa$ B requires proteolysis of the inhibitor I $\kappa$ B- $\alpha$ : Signal-induced phosphorylation of I $\kappa$ B- $\alpha$ alone does not release active NF- $\kappa$ B" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 92, pp. 552-556, (1995)
C14	Lin and Desiderio, "Regulation of V(D)J Recombination Activator Protein RAG-2 by Phosphorylation" <i>Science</i> , Vol. 260, pp. 953-959 (1993)
C15	Mellits, et al., "Proteolytic degradation of MAD3 (I $\kappa$ B $\alpha$ ) and enhanced processing of the NF- $\kappa$ B precursor p105 are obligatory steps in the activation of NF- $\kappa$ B" <i>Nucl. Acid. Res.</i> , Vol. 21, No. 22, pp. 5059-5066 (1993)
C16	Miyamoto, et al., "Tumor necrosis factor $\alpha$ -induced phosphorylation of I $\kappa$ B $\alpha$ is a signal for its degradation but not dissociation from NF- $\kappa$ B" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 91, pp. 12740-12744 (1994)

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D1	Nishizawa, M., et al., "Degradation of MOS by the N-terminal Proline (Pro2)-Dependent Ubiquitin Pathway on Fertilization of Xenopus Eggs: Possible Significance of Natural Selection for Pro2 in MOS" <i>EMBO J.</i> , Vol. 12, No. 10, pp. 4021-4027 (1993)
D2	Palombella, et al., "The Ubiquitin-Proteasome Pathway is Required For Processing the NF- $\kappa$ B1 Precursor Protein and the Activation of NF- $\kappa$ B" <i>Cell</i> , Vol. 78, pp. 773-785 (1994)
D3	Pawlak, et al., "Characterization of a Large Population of mRNAs From Human Testis" <i>Genomics</i> , Vol. 26, pp. 151-158 (1995)
D4	Pickart and Rose, "Functional Heterogeneity of Ubiquitin Carrier Proteins" <i>J. Biol. Chem.</i> , Vol. 260, No. 3, pp. 1573-1581 (1985)
D5	Read, et al., "The Proteasome Pathway Is Required for Cytokine-Induced Endothelial-Leukocyte Adhesion Molecule Expression" <i>Immunity</i> , Vol. 2, pp. 493-506 (1995)
D6	Rodriguez, M.S., et al., "Inducible Degradation of I $\kappa$ B $\alpha$ in Vitro and in Vivo Requires the Acidic C-Terminal Domain of the Protein" <i>Mol. Cell. Biol.</i> , Vol. 15(5), pp. 2413-2419 (1995)
D7	Scherer, et al., "Signal-Induced Degradation of I $\kappa$ B- $\alpha$ requires site-specific Ubiquitination" <i>Natl. Acad. Sci. USA.</i> , Vol. 92, pp. 11259-11263 (1995)
D8	Schreck, et al., "Reactive Oxygen Intermediates as Apparently Widely Used Messengers in the Activation of the NF- $\kappa$ B Transcription Factor and HIV-1" <i>EMBO J.</i> , Vol. 10 No. 8, pp. 2247-2258 (1991)
D9	Schutze, et al., "TNF Activates NF-kappa B by Phosphatidylcholine-Specific Phospholipase C-Induced "Acidic" Sphingomyelin Breakdown" <i>Cell</i> , Vol. 71 pp.765 -777
D10	Siebenlist, et al., "Structure, Regulation and Function of NF- $\kappa$ B" <i>Annu. Rev. Cell Biol.</i> , Vol. 10, pp. 405-455 (1994)
D11	Sun, et al., "NF- $\kappa$ B Controls Expression of Inhibitor I $\kappa$ B- $\alpha$ : Evidence For An Inducible Autoregulatory Pathway", <i>Science</i> , Vol. 259, pp. 1912-1915 (1993)
D12	Thanos and Maniatis, "NF- $\kappa$ B: A Lesson in Family Values" <i>Cell</i> , Vol. 80, pp. 529-532 (1995)
D13	Thévenin, et al., "Induction of Nuclear Factor- $\kappa$ B and the Human Immunodeficiency Virus Long Terminal Repeat by Okadaic Acid, A Specific Inhibitor of Phosphatases 1 and 2A" <i>New Biol.</i> , Vol. 2, pp. 793-800 (1990)
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D15	Traenckner, E.B.-M., et al, "Phosphorylation of Human I $\kappa$ B- $\alpha$ on Serines 32 and 36 Controls I $\kappa$ B- $\alpha$ Proteolysis and NF- $\kappa$ B Activation in Response to Diverse Stimuli" <i>EMBO J.</i> , Vol. 14, No. 12, pp. 2876-2883 (1995)
D16	Verma, et al., "Rel/NF- $\kappa$ B/I $\kappa$ B Family: Intimate Tales of Association and Disassociation" <i>Genes and Dev.</i> , Vol. 9 pp. 2723-2735 (1995).
D17	Wasserman, "A Conserved Signal Transduction Pathway Regulating the Activity of the Rel-Like Proteins Dorsal and NF- $\kappa$ B" <i>Mol. Biol. Cell.</i> , Vol. 4, pp. 767-771 (1993)

EXAMINER <i>C. M. Allen</i>	DATE CONSIDERED <i>2/27/01</i>
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E1	Whiteside, et al., "N- and C- Terminal Sequences Control Degradation of MAD3/I $\kappa$ B- $\alpha$ in Response to Inducers of NF- $\kappa$ B Activity" <i>Mol. Cell. Biol.</i> , Vol. 15, No. 10, pp. 5339-5345 (1995)
E2	Yaglom, et al., "p34Cdc28-Mediated Control of Cln3 Cyclin Degradation" <i>Mol. Cell. Biol.</i> , Vol. 15, No. 2, pp. 731-741 (1995)
E3	Yang, et al., "Deficient signaling in mice devoid of double-stranded RNA-dependent Protein kinase" <i>EMBO J.</i> , Vol. 14, No. 24, pp. 6095-6106 (1995)
E4	EMBL Database entry Hs369288, Accession Number N56369, from International Search Report, International Application No. PCT/US97/04195 (1996)
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